

## **REMARKS**

### **I. Status of the Claims**

With entry of this amendment, claims 1, 2, 5-8, 10-12, and 17-19 are pending and under examination. Applicant previously cancelled claims 14 and 15, and the Office has withdrawn claims 13 and 16. Applicant cancels claims 3, 4, and 9 without surrender or disclaimer of the subject matter recited therein.

Applicant has amended claims 1 and 17 to recite a probe “wherein the catalytic component is inhibited when the molecular switch is bound to an analyte.” Support for this amendment is found in the specification, for example, in Example 1.

Applicant presents new claims 18 and 19. Support for these amendments is found in the “Exemplary Embodiments” beginning on page 59 of the specification, which describe the sequences and enzymes recited in new claims 18 and 19.

No new matter is presented.

### **II. Objections to the Specification and Drawings**

#### **A. Incorporation by Reference**

The Office contends that Applicant’s amendment filed on July 28, 2006 (“Applicant’s Amendment”) introduced new matter by inserting the statement that DE 10 2004 004 882.7 and PCT/EP2005/00906, to which this application claims priority, are “incorporated herein by reference.” (Office Action, p. 3.) According to the Office, neither the national stage specification as originally filed nor PCT/EP2005/00906 contained that phrase. (*Id.*) The Office concludes the statement constitutes new matter. *Id.* The Office further notes that “37 CFR 1.57(c) and (d) explicitly state that only

nonessential material may be incorporated by reference to a foreign patent or foreign published application.” (*Id.*) (underlining in original).

Without acquiescing to the Office’s contention, and in particular, without conceding that the Office’s statement regarding nonessential material is relevant, Applicant has deleted the incorporation by reference statement from the specification solely to advance prosecution and requests the Office withdraw the objection. Applicant reserves the right under 37 CFR § 1.57 or other applicable rules, and the provisions of the Patent Act to rely on prior applications DE 10 2004 004 882.7 and PCT/EP2005/00906.

**B. 5<sup>th</sup> Exemplary Embodiment**

The Office contends that Applicant’s Amendment added new matter by amending the 5<sup>th</sup> Exemplary Embodiment from reciting “G6PDH x thrombin” to “G6PDH-5’-TGGTTGGTGTGGTTGGT-3’ - aptamer (SEQ ID NO: 4).” (Office Action, p. 3.)

Applicant disagrees. As can be seen from the specification, it refers to molecular switches using the following nomenclature: “catalytic component x target.” For example, the specification in Example 1 describes a molecular switch comprising G6PDH (catalytic component) and a nucleic acid sequence complementary to a bacteriophage  $\lambda$  nucleic acid (target). The specification describes the switch as “G6PDH x  $\lambda$ .” Specification, p. 59, lines 5-16. The 5<sup>th</sup> Exemplary Embodiment is directed to a switch for detecting thrombin using a DNA aptamer that binds thrombin. Specification, page 63, line 35 to page 38, line 17. Consequently, the “thrombin” in the name “G6PDH x thrombin” is an aptamer sequence, such as the one provided in the specification, and is not the enzyme thrombin itself. Applicant’s Amendment merely

clarified the description and did not add new matter. Nevertheless, solely to advance prosecution and without agreeing with the Office's contention, Applicant has amended the specification to restore it to the as-filed language. Applicant requests that the Office withdraw the rejection.

**C. Citation to "MA 1250"**

The Office states that Applicant's Amendment added new matter when it amended "MA 1250" to "the present specification." (Office Action, p. 4.)

Applicant disagrees, as it can be seen from the priority application that "MA 1250" is the attorney reference number for this case. Specifically, the German priority document shows "MA 1250" in the upper right-hand corner, as can be seen in the first page of that document (included with this response). It therefore follows that "MA 1250" referred to the specification, and the amendment of "MA 1250" to "the present specification" did not add new matter but added additional clarity to the sentence. Applicant requests that the Office withdraw the objection.

**D. Figures 15 and 16**

The Office objects to Figures 15 and 16, which were submitted with Applicant's Amendment. (Office Action, p. 4.) The Office contends that these figures were not in PCT Application Publication No. WO 2005/073403 A1 ("the '403 application"), to which this application claims priority, and further contends "the specific embodiments depicted in Figures 15 and 16 were not present in the PCT as originally filed." (*Id.*) According to the Office, the '403 application "refers generically" to Figures 15 and 16. (*Id.*)

Applicant respectfully disagrees. Beginning on page 36, the '403 application (corresponding to page 43 of the instant specification), provides a description of specific

embodiments immediately following the mention of Figures 15 and 16. Applicant submits that the specific embodiments depicted in Figures 15 and 16 are fully supported by the PCT application.

Nevertheless, solely to advance prosecution and without acquiescing to the objection, Applicant has canceled claims 15 and 16 and requests that the Office withdraw the objection.

### III. Claims 1-12 and 17 are Novel

#### A. *Miller*

The Office rejects claims 1-10, 12, and 17 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent Application Publication No. 2004/0018492 ("*Miller*"). (Office Action, p. 5.) According to the Office, *Miller* in Figure 6 teaches "a probe in the form of a DNA portion and a catalytic component in the form of an enzyme/inhibitor label complex, wherein the enzyme produces an electrochemical signal upon binding to a target." (*Id.* at 5-6.)

Applicant traverses. Nevertheless, solely to advance prosecution, and without acquiescing to the rejection, Applicant has amended claims 1 and 17 to recite "a molecular switch comprising a probe and a catalytic component, wherein the catalytic component is ***inhibited*** when the molecular switch is bound to an analyte." *Miller* does not anticipate claim 1, as amended, because in *Miller*, binding of the probe in Figure 6 ***activates*** the catalytic component. Accordingly, *Miller* does not disclose (or suggest) all the elements of claim 1, its dependent claims, or claim 17 and its dependent claims, and Applicant requests that the Office withdraw the rejection.

**B. *Lizardi***

The Office rejects claims 1-11 and 17 under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,118,801 (“*Lizardi*”). (Office Action, p. 7.) According to the Office, in Figures 12-13, *Lizardi* teaches a system with a probe having a ribozyme wherein “binding of a target to the probe results in a conformational switch that **activates** [the] ribozyme.” (*Id.*) (emphasis added).

Applicant traverses. As discussed above, solely to advance prosecution, and without acquiescing to the rejection, Applicant has amended claims 1 and 17 to recite “a molecular switch comprising a probe and a catalytic component, wherein the catalytic component is **inhibited** when the molecular switch is bound to an analyte.”

Accordingly, *Lizardi* does not teach (or suggest) all the elements of claim 1, its dependent claims, or claim 17 and its dependent claims, and Applicant requests that the Office withdraw the rejection.

**IV. Claims 1 and 10-12 are Nonobvious**

The Office rejects claims 1, 10, and 11 under 35 U.S.C. § 103(a) as allegedly unpatentable over *Miller* in view of *Lizardi*. (Office Action, p. 9.) The Office explains that “this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 10-11.” (*Id.*) The Office relies on its assertions regarding the teaching of *Miller* and *Lizardi*. The Office admits that *Miller* fails “to teach the catalytic component is a catalytically active nucleic acid (i.e., claims 10-11),” but contends that *Lizardi* teaches a ribozyme, which is a catalytically active nucleic acid. (*Id.* at 10.) The Office asserts that it would have been obvious to the artisan of ordinary skill in the art to modify *Miller* by substituting the catalytically active component (a proteinaceous

enzyme) with the ribozyme of *Lizardi* with a reasonable expectation of success. (*Id.*)

The Office contends that the motivation to make this substitution would have been “increasing the sensitivity of detection as a result of releasing an exponentially replicatable signal component as explicitly taught by *Lizardi*.” (*Id.*) The Office further contends that “it would have been obvious to the ordinary artisan that the known technique of using a catalytically active nucleic acid as a catalytic component on the probe as taught by *Lizardi* could have been applied to the system of *Miller*.” (*Id.* at 11.)

Applicant traverses. The Office contends that Figure 6 of *Miller* shows a system with an enzyme/inhibitor complex, wherein the enzyme is activated by binding to a target. (Office Action, pp. 10-11.)

As an initial matter, Applicant submits that the system of *Miller* would not work as *Miller* intended if the probe were active in the absence of binding to target and then inhibited upon binding. Figure 6 of *Miller* purports to describe a system where binding of probe activates the enzyme, and is detected by measuring the appearance of product of the enzyme. *Miller*, paragraph [050]. If the probe were active before binding, however, the product of the enzyme would already be present in the assay system. Thus, to detect inhibition of the enzyme, one would first have to separate away the product of the enzyme in order to measure inhibition (i.e., the absence or reduction of product of the enzyme upon binding to the target). But *Miller* explains that Figure 6 describes a system where separation of components is not necessary. *Id.* Thus, a probe wherein the catalytic component is inhibited when the molecular switch is bound to an analyte is contrary to *Miller*'s express teaching.

Moreover, the Office, however, has not explained how one of skill in the art could make a ribozyme/inhibitor complex by substituting the proteinaceous enzyme of *Miller* for the ribozyme of *Lizardi*, such that binding to target would activate the ribozyme. More specifically, the Office has not provided any evidence or reasoning that an inhibitor of a proteinaceous enzyme could be used to inhibit a ribozyme, which is a nucleic acid. As explained by *Lizardi* in Example V and Figure 12, whether a nucleic acid forms an active ribozyme depends on the structure of the nucleic acid. The Office has not explained how the inhibitor of *Miller* could modulate the structure of the nucleic acid of *Miller* to inhibit formation of an active ribozyme, or provided any evidence that one of skill in the art would have expected it to do so. Accordingly, Applicant submits that the Office has not established *prima facie* obviousness as the Office has not shown that the skilled artisan would have reasonably expected the ribozyme of *Lizardi* to be substitutable with the proteinaceous enzyme of *Miller*. Applicant requests that the Office withdraw the rejection.

The Office also rejects claims 1, 10, and 12 under 35 U.S.C. § 103(a) as allegedly unpatentable over *Lizardi* in view of *Miller*. (Office Action, p. 11.) The Office notes that “this rejection applies to claim 1 to the extent it is drawn to the embodiments of dependent claims 10 and 12.” (*Id.*) The Office relies on its assertions regarding the teachings of *Miller* and *Lizardi*, but admits that “*Lizardi* does not teach the catalytically active component is an enzyme.” (*Id.* at 11-12.) The Office, however, contends that *Miller* teaches an enzyme, and that it would have been obvious to the skilled artisan to have modified the system of *Lizardi* by substituting the catalytic component (ribozyme) for the enzyme of *Miller*. (*Id.* at 12.)

Applicant traverses and submits that the Office has not shown that the skilled artisan would have reasonably expected the substitution of *Miller's* proteinaceous enzyme for *Lizardi's* ribozyme to work. Specifically, the probe of *Lizardi* inhibits the catalytic component when it is bound to target, because binding changes the structure of the probe. See Figure 12. As explained by *Lizardi*, for *Lizardi's* probes to be functional, they require “three essential elements,” including “switch sequences” that form a ribozyme when in the proper configuration. See *Lizardi* Abstract and Figure 12. The Office has provided no evidence that the skilled artisan would have reasonably expected success in removing “essential elements” (“the switch sequences”) and substitution those “essential elements” for a proteinaceous enzyme. Consequently, Applicant submits that the Office has not established *prima facie* obviousness and requests that the Office withdraw the rejection.

## **V. Conclusion**

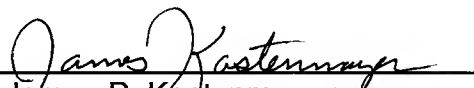
In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

If there is any fee due in connection with the filing of this Statement, please  
charge the fee to Deposit Account 06-0916.

Respectfully submitted,

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